

GRAM – POSITIVE COCCI

GENUS: STREPTOCOCCUS



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10. 2. 15.

مركز الشامل للخدمات الطلابية

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Streptococcus Agalactiae

in female vagina

neonatal

sepsis

STREPTOCOCCUS



Streptococci

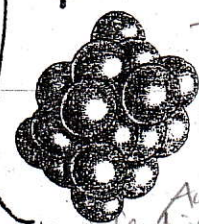
Streptococci of medical importance are listed in table 15-3, all but one of these streptococci are discussed here; Streptococcus pneumoniae is discussed separately at the end of this chapter.

Diseases Streptococci causes a wide variety of infections. S pyogenes (group A streptococcus) is the leading bacterial cause of pharyngitis and cellulitis. It also induces two important immunologic diseases, namely, rheumatic fever and acute glomerulonephritis. S agalactiae (group B streptococcus) is the leading cause of neonatal sepsis and meningitis. Enterococcus faecalis is an important cause of hospital-acquired urinary tract infections. Viridans group streptococci are the most common cause of endocarditis. S bovis also causes endocarditis.

neonatal sepsis
in female vagina
caused Streptococcus Pyogenes



STREPTO-STAPHYLODERMIA



Post Streptococcal complication
Throat infection
Acute Rheumatic fever
Autoimmune
Skin infection
Kidney immune complex deposition
Acute glomerular nephritis

Throat

Streptococcus Pyogenes group A

Streptococcus

pharyngitis

* Bacitracin: an Antibiotic obtained from *Bacillus subtilis*. Its Antibacterial Action is similar to those of Penicillin. It treats gram positive cocci and bacilli and some gram negative organisms because Bacitracin is toxic when used parenterally it is usually applied topically in ointment form.

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Important properties Streptococci are spherical Gram – positive cocci arranged in chains or pairs. All streptococci are catalase – negative, whereas staphylococci are catalase – positive (Table 15-3).

One of the most important characteristics for identification of streptococci is the type of hemolysis. AEROBES AND FACULTATIVE-ANAEROBES.

- (1) **Alpha – hemolytic** streptococci form a green zone around their colonies as a result of incomplete lysis of red blood cells in the agar.
- (2) **Beta- hemolytic** streptococci form a clear zone around their colonies because complete lysis of the red cells occurs. Beta-hemolysis is due to the production of enzymes (hemolysins) called streptolysin O and streptolysin S (see the pathogenesis section below).
- (3) Some streptococci are nonhemolytic (gamma – hemolysis).

TABLE 15-3, STREPTOCOCCI OF MEDICAL IMPORTANCE.

SPECIES	LANCEFIELD GROUP	TYPICAL HEMOLYSIS	DIAGNOSTIC FEATURES ¹
1. <i>S pyogenes</i>	A	<u>Beta</u>	Bacitracin-sensitive
2. <i>S agalactiae</i>	B	<u>Beta</u>	Bacitracin- <u>resistant</u> ; hippurate hydrolyzed
3. <i>S faecalis</i> ² <i>enterococcus faecalis</i>	D	<u>Alpha or beta or none</u>	Growth in 6.5% NaCl. ³ ; <u>40% bile</u>
4. <i>S bovis</i>	D	Alpha or none	<u>No growth in 6.5% NaCl.</u>
5. <i>S pneumoniae</i>	NA ⁴	Alpha	Bile – soluble ; inhibited by <u>optochin</u> .
6. Viridans group	NA	Alpha	Not bile – soluble ; not inhibited by <u>optochin</u> .

¹ All streptococci are catalase – negative.

7. *Streptococcus thermophilus*: NON-GROUP, α -haemolytic, is used as START CULTURE in MAKING YOGURT.
8. *Streptococcus cremoris*: α or γ -hemolytic, GROUP-N, START CULTURES in CHEESE – MANUFACTURING.
9. *Streptococcus lactis*: α or γ -haemolytic, GROUP-N, CAUSES COAGULATION, SOURING, AND SPOILAGE OF MILK.

JK

Lansfield divided all streptococci according to carbohydrate

To differentiate between *Streptococcus pneumoniae* and *Streptococcus viridans* we test by optochin if the growth of streptococci is inhibited then it's *S. pneumoniae* if it's not inhibited then it's *S. viridans*.

Some chemical characteristics and cellular location of streptococcal antigens

Group antigen (hapten)			Type antigen (hapten)			Species
Designation	Chemical nature	Cellular location	Designation	Chemical nature	Cellular location	
A	Rhamnose-N-acetyl-glucosamine polysaccharide	Wall	M R T	Protein Protein Protein	Envelope Envelope Envelope	<i>S. pyogenes</i>
B	Rhamnose-glucosamine polysaccharide	Wall	S (5 types)	Glucose-galactose-N-acetyl-glucosamine polysaccharide	Envelope	<i>S. agalactiae</i>
C	Rhamnose-N-acetyl-galactosamine polysaccharide	Wall	(8 types described) (3 types) (Only 1 type described) (3 types)	Protein Protein Protein Protein	Envelope	<i>S. equisimilis</i> <i>S. zooepidemicus</i> <i>S. equi</i> <i>S. dysgalactiae</i>
D	Glycerol teichoic acid containing D-alanine and glucose	"Intracellular" between wall and membrane	(11 types established) (19 types described; many more exist)	Rhamnose-glucosamine-glucose polysaccharide	Cell wall	<i>S. faecalis</i> <i>S. faecium</i>
D, Q			(Many types exist)	Carbohydrate?	Capsule	<i>S. avium</i> <i>S. bovis</i> <i>S. equinus</i> <i>Streptococcus</i> sp.
E	Rhamnose polysaccharide	Wall	I to V	Polysaccharide		<i>S. anginosus</i>
F	Rhamnose and a glucopyranosyl-N-acetyl-galactosamine tetrasaccharide	Wall	I to V	Carbohydrates—some types contain glucose, galactose and rhamnose		<i>Streptococcus</i> sp. (large colony)
G	Rhamnose-galactosamine polysaccharide	Wall	(3 types described)			<i>S. sanguis</i>
H	Rhamnose polysaccharide	Wall	(5 types described)			<i>Streptococcus</i> sp., <i>S. salivarius</i>
K	Rhamnose polysaccharide	Wall	I and II, and I-II	Galactose, glucose rhamnose Type I—O-β-D galactopyranosyl-(1→6)-D-galactose	Cell wall	
N	Glycerol teichoic acid containing D-alanine and galactose phosphate	"Intracellular" between wall and membrane	Many types exist			<i>S. lactis</i> — milk <i>S. cremoris</i> — cheese
D			(Only 1 type)	Contains glucose, glucosamine, galactosamine	Capsule	<i>S. suis</i>
None	Ribitol teichoic acid with choline phosphate	Wall	(80 types) M	Carbohydrate Protein	Capsule Envelope	<i>S. pneumoniae</i>

Enterococcus faecalis growth in 6.5 NaCl and 40% Bile

3

oral
strep
Subacute Bacterial endocarditis
from tooth extraction not given prophylactic Amoxicillin

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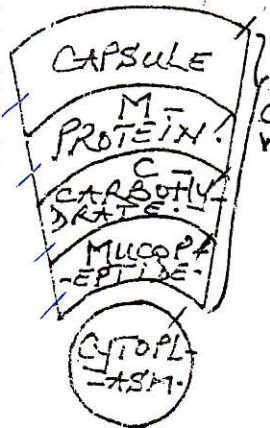
Serotype: in Microbiology a microorganism determined by the kinds and combination of Antigens present on its cell surface

How to detect the S. faecalis and S. bovis?

- ² Now called Enterococcus faecalis and abbreviated enterococci; S bovis is a nonenterococcal group D organism.
- ³ Both S faecalis and S bovis grow on bile - esculin agar, whereas other streptococci do not. They hydrolyze the esculin, and this results in a characteristic black discoloration of the agar.
- ⁴ NA, not applicable.

S. pyogenes and Agalactiae

There are two important antigens of beta - hemolytic streptococci:
Lancefield groups



- (1) C carbohydrate determines the group of beta - hemolytic streptococci. It is located in the cell wall, and its specificity is determined by an amino sugar.
- (2) M protein is the most important virulence factor and determines the type of group A beta - hemolytic streptococci. It protrudes from the outer surface of the cell and interferes with ingestion by phagocytes; ie, it is antiphagocytic. Antibody to M protein provides type - specific immunity. There are approximately 80 serotypes based on the M protein, which explains why multiple infections with S pyogenes can occur. Strains of pyogenes that produce certain M-protein types are rheumatogenic, ie, cause primarily rheumatic fever, whereas strains of S pyogenes that produce other M protein types are nephritogenic, ie, cause primarily acute glomerulonephritis. Although M protein is the main antiphagocytic component of S pyogenes, the organism also has a polysaccharide capsule that plays a role in retarding phagocytosis.

- 1-Pharyngitis
- 2-Cellulitis
- 3-Erysipelas
- 4-impetigo
- 5-otitis media
- 6-pneumonia
- 7-sore throat
- 8-necrotizing fasciitis
- 9-sepsis
- 10-sinusitis
- 11-tonsillitis
- 12-Rheumatic fever
- 13-Acute glomerulonephritis

Hydrolytic acid capsule

The classification of streptococci is as follows.

- A. Beta - hemolytic streptococci : these are arranged into groups A-U (known as Lancefield groups) on the basis of antigenic

4

Rheumatic fever

Some strains of S. pyogenes are Rheumatogenic and other nephritogenic.

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↓
Primarily Acute glomerulonephritis

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A - *S. Pyogenes*
B - *S. Agalactiae*

Precipitation test:
a test in which two dissolved substances in solution join to form a visible solid. The result depends on the strength of attraction between the Fab fragment on the antibody and the corresponding epitope on the antigen.

differences in C carbohydrate. In the clinical laboratory, the group is determined by precipitin tests with specific antisera or by immunofluorescence.

Group A streptococci (*Streptococcus pyogenes*) are among the most important human pathogens. They are the most frequent bacterial cause of pharyngitis. They adhere to pharyngeal epithelium via pili covered with lipoteichoic acid and M protein. Many strains have a hyaluronic acid capsule that is antiphagocytic. They are usually **bacitracin - susceptible**, an important diagnostic criterion.

bacitracin +
in *S. pyogenes*.

Group B streptococci (*Streptococcus agalactiae*) colonize the genital tract of some women and can cause neonatal meningitis and sepsis. They are usually bacitracin-resistant.

Group D streptococci include enterococci (eg, *Enterococcus faecalis* and *Enterococcus faecium*) and nonenterococci (eg, *Streptococcus bovis*). Enterococci grow in 6.5% NaCl and are not killed by penicillin G, grow in 40% bile salt and tolerate 45°C for 30 minutes. they occur as part of the normal flora in the gut and are noted for their ability to cause urinary, biliary, and cardiovascular infections. Nonenterococci can produce similar infection but are inhibited by 6.5% NaCl and are killed by penicillin G. Note that the hemolytic reaction of group D streptococci is variable: some are beta-hemolytic, whereas most are alpha-hemolytic or non hemolytic.

viridans group
S. mutans
S. sanguis
S. mitis
S. salivarius
S. oralis.

Groups C, E, F, G, H, and K - U streptococci infrequently cause human disease.

Group N "lactic" streptococci produce normal souring of milk.

B. Non - Beta - Hemolytic Streptococci: Some produce no hemolysis; others produce alpha hemolysis. The principal alpha-hemolytic organisms are *S. pneumoniae* and the viridans group of streptococci. The viridans streptococci (eg, *Streptococcus mitis*, *S. sanguis*, and *S. mutans*) are not bile soluble and not inhibited by optochin - in contrast to *S. pneumoniae*. Viridans streptococci are part of the normal flora

The principal
α-hemolytic
streptococci
are
S. pneumoniae
and
S. viridans

S. salivarius, *S. oralis*,

Think of group B streptococci as baby → *S. agalactiae* Present in the vagina of women during delivery → Sepsis, Pneumonia, meningitis of the newborn.

Imp
Endocarditis:
infection or inflammation of heart valves
or lining of the heart.

of the human pharynx and intermittently reach the bloodstream to cause infective endocarditis. *S mutans* synthesizes polysaccharides (dextrans) that are found in dental plaque and lead to dental caries. *Streptococcus intermedius* and *Streptococcus anginosus* (also known as the *Streptococcus anginosus - milleri* group) are usually alpha-hemolytic or nonhemolytic, but some isolates are beta-hemolytic. They are found primarily in the mouth and colon.

C. **Peptostreptococci**: these grow under anaerobic or microaerophilic conditions and produce variable hemolysis. Peptostreptococci are members of the normal flora of the gut and the female genital tract and participate in mixed anaerobic infection. NON - GROUP.

Transmission Most streptococci are part of the normal flora of the human: throat, skin, and intestines but produce disease when they gain access to tissues or blood. Viridans streptococci and *S pneumoniae* are found chiefly in the oropharynx; *S pyogenes* found on the skin and in the oropharynx in small numbers; *S agalactiae* occurs in the female genital tract; and both the enterococci and anaerobic streptococci are located in the lower intestinal tract.
Peptostreptococci.

Pathogenesis group A streptococci (*S pyogenes*) cause disease by three mechanisms: (1) inflammation, which is induced locally at the site of the organisms in tissue; (2) exotoxin production, which can cause widespread systemic symptoms in areas of the body where there are no organisms; and (3) immunologic, which occurs when antibody against a component of the organism cross-reacts with normal tissue or forms immune complexes that damage normal tissue (see the section on poststreptococcal disease below). (fig 30.2).

Group A streptococci produce eight important toxins and enzymes.

- 3 enzymes 8
5 Toxins and Hemolysins
- 1- Streptokinase
 - 2- Hyaluronidase
 - 3- DNase
 - 4- exotoxin B
 - 5- erythrogenic toxin
 - 6- streptococcal exotoxin
 - 7- streptolysin O
 - 8- streptolysin S

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120
150
180
330

Plasminogen → Plasmin
Streptokinase → clot destruction
S. pyogenes

S. pyogenes → Streptolysin
→ DNase
→ Hyaluronidase

A. INFLAMMATION - RELATED ENZYMES

- (1) Streptokinase (fibrinolysin) activate plasminogen to form plasmin, which dissolves fibrin in clots, thrombi, and emboli. It can be used to lyse thrombi in the coronary arteries of heart attack patients.
- (2) DNase (streptodornase) depolymerizes DNA in exudates or necrotic tissue. Antibody to DNase B develops during pyoderma; this can be used for diagnostic purposes. Streptokinase - streptodornase mixtures applied as a skin test give a positive reaction in most adults, indicating normal cell-mediated immunity. DNase gives rise to watery non-viscous pus, in contrast to Staph. aureus highly viscous pus.
- (3) Hyaluronidase degrades hyaluronic acid, which is the ground substance of subcutaneous tissue. Hyaluronidase is known as spreading factor because it facilitates the rapid spread of S pyogenes in skin infections (cellulites).

scarlet rash
a rose coloured
rash
like
in Gherkin
members

Pyoderma:
any acute inflammatory
dermatitis
قشر

Dick test: a technique

B. Toxins and hemolysins

- (4) Erythrotoxic erythrogenic toxin causes the rash of scarlet fever. Its mechanism of action is similar to that of the toxic shock syndrome toxin (TSST) of S aureus; it acts as a superantigen (see S aureus. above, and chapter 58). It is produced only by certain strains of Streptococcus pyogenes lysogenized by a bacteriophage carrying the gene for the toxin. The injection of a skin test dose of erythrogenic toxin (Dick test) gives a positive result in persons lacking antitoxin (ie. susceptible persons). IT IS AN ACUTE

Bacteriophage:
a virus that infects
and lyses bacteria.
it consists of a
head that contains
either DNA or RNA
and a tail by which
it attaches to
the host cell.

Cellulites:
as spreading bacterial
infection of skin and
SK tissues.

scarlet
fever

NEPHARYNGITIS AND ACUTE-TONSILLITIS WITH
HIGH- FEVER PLUS BODY-RASH → NECK, UPPER-
CHEST AND BACK → TRUNK AND EXTREMITIES.
OCCURS IN NON- IMMUNE PERSONS.
CAUSED BY M - 7 TYPES 1, 3, 12 AND 28.

* superAntigen: an Antigen that binds with class I MHC Antigens and T-cell receptors causes the simultaneous release of cytokines. such antigens don't have to be processed by Macrophages to be recognized by T cells. exotoxins from Bacteria such as staph. aureus and group A Strept act as superAntigen. A superAntigen known as toxic shock syndrome toxin-1 causes toxic shock syndrome

Anti streptolysin
An antibody that
opposes the action
of streptolysin.

a.O ASLO.
using streptolysin
that is used
retrospectively to
diagnose
infections with
group A beta
hemolytic
streptococci.

TSS:
a rare disorder similar to
septic shock caused
by exotoxin produced
by certain strains of
S. aureus and group A
strept. It was originally
described in young women
using vaginal tampons
but has also been
reported in users of
contraceptive sponges
and diaphragms and after
surgical wound packing.

Symptoms:
- Fever 38-40°C
- Diffuse macular flat
erythematous rash
followed in 1 or 2
weeks by peeling of
the skin
- Hypotension
- Orthostatic syncope
- Vomiting
- Severe myalgia
- Hyperemia
- Platelet less
than 100,000/mm³

Treatment
Penicillase resistance antibiotics
such as nafcillin or oxacillin don't
affect the initial syndrome but may
prevent recurrence.
Supportive care (i.v. fluids, pressor drugs)
LC is provided.

(5) **Streptolysin O** is a hemolysin that is inactivated by oxidation (oxygen - labile). It causes beta-hemolysis only when colonies grow under the surface of a blood agar plate. It is antigenic and antibody to it (ASO) develops after group A streptococcal infections. The titer of ASO antibody can be important in the diagnosis of rheumatic fever.

(6) **Streptolysin S** is a hemolysin that is not inactivated by oxygen (oxygen-stable). It is not antigenic but is responsible for beta-hemolysis when colonies grow on the surface of a blood agar plate.

(7) **Pyrogenic exotoxin A** is the toxin responsible for most cases of streptococcal toxic shock syndrome. It has the same mode of action as does staphylococcal TSST: ie, it is a superantigen that causes the release of large amount of cytokines from helper T cells and macrophages (see p 87 and chapter 7 and 58).

↓ class I MHC binds to

Exotoxin B is a protease that rapidly destroys tissue and is produced in large amounts by the strains of S pyogenes that cause necrotizing fasciitis.

Phagogenesis by group B streptococci (*Streptococcus agalactiae*) is based on the ability of the organism to induce an inflammatory response. However, unlike *Streptococcus pyogenes*, no enzymes or exotoxins have been described and there is no evidence for any immunologically induced disease. Group B streptococci have a polysaccharide capsule that is antiphagocytic, and anticapsular antibody is protective.

Clinical findings S pyogenes causes three types of disease :

(1) **pyogenic** disease such as pharyngitis and cellulitis, (2) **toxigenic** diseases such as scarlet fever and toxic shock syndrome, and

Pyrogenic exotoxin B

8

Necrotizing fasciitis: a severe bacterial infection that spreads rapidly through the body along superficial and deep fascial planes, resulting in necrosis of SIC and extensive undermining Hospital gangrene.

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non supportive
 Rheumatic fever, Acute glomerular nephritis?
 Streptococcus pyogenes
 cause 3 types of disease
 Pyogenic, toxicogenic, Immunologic

(3) **immunologic** disease such as rheumatic fever and acute glomerulonephritis. (see the section on poststreptococcal diseases, below).

S pyogenes (group A beta - hemolytic streptococcus) is the most common bacterial cause of sore throat. Pharyngitis is characterized by inflammation, exudates, fever, leukocytosis, and tender cervical lymph nodes. If untreated, spontaneous recovery occurs in 10 days. However, it may extend to otitis, sinusitis, mastoiditis, and meningitis. If the infecting streptococci produce erythrogenic toxin and the host lacks antitoxin, scarlet fever may result. Rheumatic fever may occur, especially following pharyngitis. S. pyogenes also causes another toxin, mediated disease, streptococcal toxic shock syndrome, which has clinical findings similar to those of staphylococcal toxic shock syndrome.

Group A streptococci can enter skin defects to produce cellulitis, (fig 6) erysipelas (fig 12), necrotizing fasciitis (streptococcal gangrene), lymphangitis, or bacteremia. They can enter the uterus after delivery to produce endometritis and sepsis (puerperal fever), the most highly fatal from is caused by streptococcus pyogenes among all other bacteria. Streptococcal pyoderma (impetigo) is a superficial infection of abraded skin that forms pus or crusts. It is communicable among children, especially in hot, humid climates. Glomerulonephritis may occur, especially following skin infections.

Group B streptococci cause neonatal sepsis and meningitis. The main predisposing factor is prolonged (longer than 18 hours), rupture of the membranes in women who are colonized with the organism. Children born prior to 37 weeks gestation have a greatly increased risk of disease. Also children whose mothers who lack antibody to group B streptococci and who consequently are born without transplacentally acquired IgG have a high rate of neonatal sepsis caused by this organism although most group B streptococcal infection are in neonates. this organism also causes such infections as pneumonia, endocarditis, arthritis, and osteomyelitis in

NOTE: Streptococcus iniae is also called "FLESH-EATING-BACTERIUM"

1994 - ENGLAND
 1998 - TEXAS - U.S.A.

Pyogenic infectious all of them?

non immun

Arthritis

Hyaluronidase Action

Exotoxin B
 Protease Action

Scarlet fever
 Erysipelas: an infection of the skin usually caused by group A strept that is marked by bright red swollen sharply defined rash that stings or itches on the face, scalp, arms, legs or trunk

Erysipylis

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Group B streptococcus infections in adults
1- osteomyelitis
2- arthritis
3- pneumonia
4- endocarditis
↑
Prehospital factor DM

adults. Postpartum endometritis also occurs. Diabetes is the main predisposing factor for adult group B streptococcal infections.

Viridans streptococci (eg, *S mutans*, *S sanguis*, and *S mitis*) are the most common cause of infective endocarditis. They enter the bloodstream from the oropharynx, typically after dental surgery. Signs of endocarditis are fever, anemia, heart murmur, and embolic events. It is 100% fatal unless effectively treated with antimicrobial agents. About 10% of endocarditis cases are caused by Enterococci, but any organism causing bacteremia may settle on deformed valves. At least three blood cultures are necessary to ensure recovery of the organism in more than 90% of cases (fig 30.2).

UTI Hospital acquired infections

Enterococci cause urinary tract infections, especially in hospitalized patients. Indwelling urinary catheters and urinary tract instrumentation are important predisposing factors. Enterococci also cause endocarditis, particularly in patients who have undergone gastrointestinal or urinary tract surgery or instrumentation. They also cause intra - abdominal and pelvic infections, typically in combination with anaerobes. *Streptococcus bovis*, a nonenterococcal group D streptococcus, causes endocarditis, especially in patients with carcinoma of the colon. This association is so strong that patients with *S bovis* bacteremia or endocarditis should be investigated for the presence of colonic carcinoma.

Streptococcus intermedius and *streptococcus anginosus* cause dental, brain, and abdominal abscesses and endocarditis. Peptostreptococci participate in mixed anaerobic infections of the abdomen, pelvis, lungs, and brain and after teeth extraction.

Poststreptococcal (Nonsuppurative) Diseases These are disorders in which a local infection with group A streptococci is followed weeks later by inflammation in an organ that was not infected by the streptococci. The inflammation is caused by an **immunologic** response to streptococcal M proteins that cross - react with human tissues. Some

* SUBACUTE BACTERIAL ENDOCARDITIS.

strains of *S. pyogenes* bearing certain M proteins are nephritogenic and cause acute ^{AGN} glomerulonephritis, and other strains bearing different M proteins are rheumatogenic and cause acute rheumatic fever.

A. Acute glomerulonephritis: Acute glomerulonephritis (AGN) typically occurs 2-3 weeks after skin infection by certain group A streptococcal types in children (eg, M protein type 49 causes AGN most frequently). AGN is more frequent after skin infections than after pharyngitis. The most striking clinical features are hypertension, edema of the face (especially periorbital edema) ankles, and "smoky urine (due to red cells in the urine). Most patients recover completely. Reinfection with streptococci rarely leads to recurrence of acute glomerulonephritis. (No Reactivation).

The disease is initiated by antigen - antibody complexes on the glomerular basement membrane, and soluble antigens from streptococcal membranes may be the inciting antigen. It can be prevented by early eradication of nephritogenic streptococci from skin colonization sites but not by administration of penicillin after onset of symptoms.

B. Acute rheumatic fever: Approximately 2 weeks after any type of group A streptococcal infection - usually pharyngitis- rheumatic fever, characterized by fever, migratory polyarthritides, and carditis. may develop. The carditis damages myocardial and endocardial tissue, especially the mitral and aortic valves. ASO titers and the erythrocyte sedimentation rate are elevated. ESR

Rheumatic fever is due to an immunologic reaction between cross-reacting antibodies to certain streptococcal M proteins and antigen of joint and heart tissue (FIG 30.2). It is an autoimmune disease, greatly exacerbated by recurrence of streptococcal infections. If streptococcal infections are treated within 8 days of onset, rheumatic fever is usually

عريسيپيلاس (erysipelas) . GREEK = ERYTHROS = RED, AND PELLA FOR SKIN.

Is a febrile disease, characterized by inflammation and redness of the skin. Inflammation can attack mucous membranes and subcutaneous tissues. Complications :

1. Gangrene and
2. Lymphatic obstruction.

Fig: 15 ERYSIPELAS of the leg

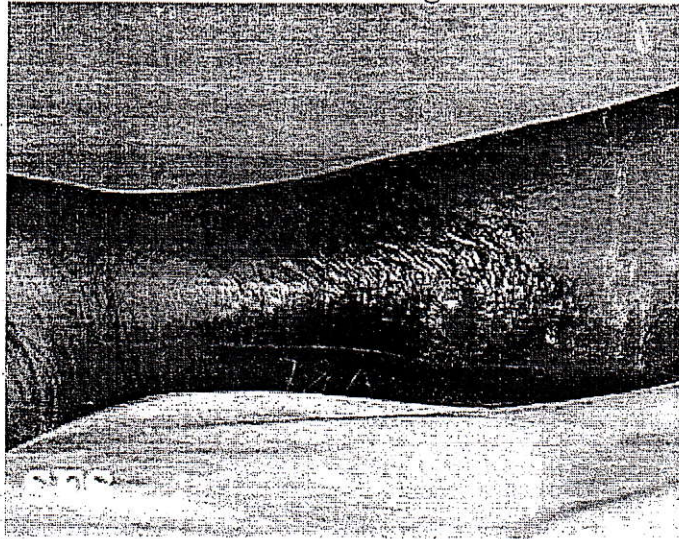


Fig: 16 ERYSIPELAS of the face



Flesh Eating Disease

Is a fatal septicemic disease of skin, subcutaneous tissues and muscles, complicated by gangrene, septicemia, shock and death. It is caused by a new mutant of *Streptococcus pyogenes* called :- *Streptococcus* *Siniae*.



Fig 13- Necrotizing cellulitis developed in the right thigh and lower abdomen in this patient

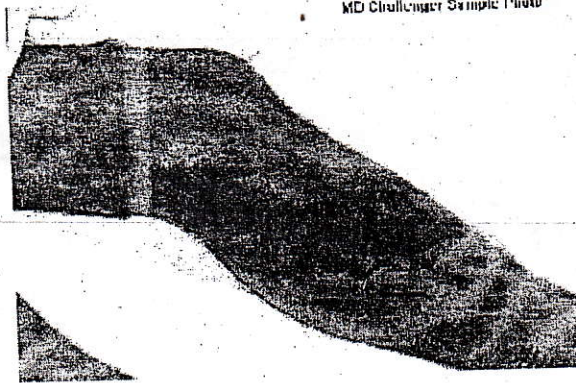


Fig 14 Necrotizing cellulitis developed in the left leg in this patient

FLESH - EATING - DISEASE.



- Streptococcus iniae.

Fortunately, approximately every 10-years, a new - mutant of Streptococcus gains dominance; perhaps the flesh-eating strain is nearing the end of its 10-year-cycle. ◀

prevented. After a heart- damaging attack of rheumatic fever, reinfection must be prevented by long – term prophylaxis (**Reactivation Occurs**). In the United States, fewer than 0.5% of group A streptococcal infections lead to rheumatic fever, but in developing tropical countries, the rate is higher than 5%.

LABORATORY DIAGNOSIS

A. **Microbiologic** : Gram – stained smears are useless in streptococcal pharyngitis because viridans streptococci are members of the normal flora and cannot be visually distinguished from the pathogenic *S. pyogenes*. However, stained smears from skin lesions or wounds that reveal streptococci are diagnostic. Cultures of swabs from the pharynx or lesion on blood agar plates show small, translucent beta-hemolytic colonies in 18 – 48 hours. If inhibited by bacitracin disk, they are likely to be group A streptococci. Group B streptococci are characterized by their ability to **hydrolyze hippurate** and by the production of a protein that causes enhanced hemolysis on sheep blood agar when combined with beta – hemolysin of *S. aureus* (CAMP test). Group D streptococci **hydrolyze esculin in the presence of bile**; ie, they produce a black pigment on bile – esculin agar. The group D organisms are further subdivided: the enterococci grow in hypertonic (6.5%) NaCl, whereas the nonenterococci do not. (Tables 15-4A, 15-4B, Fig 33).

Although cultures remain the gold standard for the diagnosis of streptococcal pharyngitis, a problem exists because the results of culturing are not available for at least 18 hours and it is beneficial to know while the patient is in the office whether antibiotics should be prescribed. For this reason, rapid tests that provide a diagnosis in approximately 10 minutes were developed. The rapid test detects

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bacterial antigens in a throat swab specimen. In the test, specific antigens from the group A streptococci are extracted from the throat swab with certain enzymes and are reacted with antibody to these antigens bound to latex particles occurs if group A streptococci are present in the throat swab.

B. Serologic : ASO titers are high soon after group A streptococcal infections. In patients suspected of having rheumatic fever, an elevated ASO titer is typically used as evidence of previous infection because throat culture results are often negative at the time the patient present with rheumatic fever. Titters of anti - DNase B are high in group A streptococcal skin infections and serve as an indicator of previous streptococcal infection in patients suspected of having AGN.

↑ ASO
↑ Anti-DNase B

streptokinase-streptolysin
titers

Treatment All group A streptococci are susceptible to penicillin G, but neither rheumatic fever nor AGN patients benefit from penicillin treatment after onset. In mild group A streptococcal infections, oral penicillin V can be used. In penicillin - allergic patients, erythromycin or one of its long acting derivatives, eg, azithromycin, can be used. Endocarditis caused by most viridans streptococci is curable by prolonged penicillin treatment. However, enterococcal endocarditis can be eradicated only by a penicillin or vancomycin combined with an aminoglycoside. Enterococci resistant to multiple drugs, eg, penicillin, aminoglycosides, and vancomycin, have emerged. Vancomycin - resistant enterococci (VRE) are now an important cause of nosocomial infections; there is no reliable antibiotic therapy for these organisms. (in april 2000 , the FDA approved linezolid [Zyvox] for the treatment of infections caused by VRE.) nonenterococcal group D streptococci, eg, S bovis, are not highly resistant and can be treated with penicillin G. The drug of choice for group B streptococcal infections is penicillin G. Some strains may require higher doses of penicillin G or a

F.D.A = Food and Drug Administration - U.S.A.

إدارة الدواء والغذاء الأمريكية

combination of penicillin G and an aminoglycoside to eradicate the organism. Peptostreptococci can be treated with penicillin G.

Prevention Rheumatic fever can be prevented by prompt treatment of group A streptococcal pharyngitis with penicillin. Prevention of streptococcal infections (usually with benzathine penicillin once each month of several years) in persons who have had rheumatic fever is important to prevent recurrence of the disease. There is no evidence that patients who have had AGN require similar penicillin prophylaxis.

In patients with damaged heart valves who undergo invasive dental procedures, endocarditis caused by viridans streptococci can be prevented by using amoxicillin perioperatively. In patients with damaged heart valves who undergo gastrointestinal or urinary tract procedures, endocarditis caused by enterococci can be prevented by using ampicillin and gentamicin perioperatively.

enterococci
faecalis

Neonatal sepsis caused by group B streptococci can be prevented by administration of parenteral ampicillin perinatally to women who experience prolonged (longer than 18 hours) rupture of membranes, whose labor begins before 37 week's gestation, or who have a fever at the time of labor. Oral ampicillin given to women who are vaginal carriers of group B streptococci does not eradicate the organism. Rapid screening tests for group B streptococcal antigens in vaginal specimens are insensitive and neonates born of antigen - negative women have, nevertheless, developed neonatal sepsis.

There are no vaccines available against any of the streptococci described in the section above.

مركز الشامل للخدمات الطلابية

STREPTOCOCCUS PNEUMONIAE.

Diseases Pneumococci cause pneumonia, bacteraemia, meningitis, and infections of the upper respiratory tract as otitis and sinusitis.

Important properties Pneumococci are Gram – positive lanceolate – shaped cocci arranged in pairs (diplococci) or short chains. (The term “ lanceolate – shaped” means that the diplococci are oval with somewhat pointed ends rather than being round). On blood agar they produce alpha-hemolysis. In contrast to viridans streptococci, they are lysed by bile or deoxycholate and their growth is inhibited by optochin.

Pneumococci possess **polysaccharide capsules** of more than 85 antigenically distinct types. With type – specific antiserum, capsules swell (**quellung reaction**), and this can be used to identify the type. Capsules are virulence factors ; ie, they interfere with phagocytosis and favor invasiveness. Specific antibody to the capsule opsonizes the organism, facilitates phagocytosis, and promotes resistance. Such antibody develops in humans as result either of infection (asymptomatic or clinical) or of administration of polysaccharide vaccine. Capsular polysaccharide elicits primarily a B cell (ie, T – independent) response.

Transmission Humans are the natural hosts for pneumococci, there is no animal reservoir. Because a proportion (40-70 %) of the healthy population harbor virulent organisms in the oropharynx, pneumococcal infections are not considered to be communicable. Resistance is high in healthy young people, and disease results most often when predisposing factors (see below) are present).

Pathogenesis The most important virulence factor is the capsular polysaccharide, and anticapsular antibody is protective. Lipoteichoic acid,

which activates complement and induces inflammatory cytokine production, contributes to the inflammatory response and to the septic shock syndrome that occurs in some immunocompromised patients. Pneumolysin, the hemolysin that causes alpha hemolysis, may also contribute to pathogenesis. Pneumococci produce IgA protease that enhances the organism's ability to colonize the mucosa of the upper respiratory tract. Pneumococci multiply in tissues and cause inflammation. When they reach alveoli, types 1-8 cause 75% of pneumococcal pneumonias. There is outpouring of fluid and red and white blood cells, resulting in consolidation of the lung. During recovery, pneumococci are phagocytized, mononuclear cells ingest debris, and the consolidation resolves.

FACTORS THAT LOWER RESISTANCE AND PREDISPOSE PERSONS TO PNEUMOCOCCAL INFECTION INCLUDE (1) alcohol or drug intoxication or other cerebral impairment that can depress the cough reflex and increase aspiration of secretions ; (2) abnormality of the respiratory tract (eg, viral infections), pooling of mucus, bronchial obstruction (atelectasis) , and respiratory tract injury caused by irritants (which disturb the integrity and movement of the mucociliary blanket); (3) abnormal circulatory dynamics (eg, pulmonary congestion and heart failure) ; (4) **splenectomy** ; and (5) certain chronic disease such as sickle cell anemia and nephrosis. Trauma to the head that causes **leakage of spinal fluid** through the nose predisposes to pneumococcal meningitis. Frequent types affecting children are 6, 14, 19 and 23.

Clinical Findings Pneumonia often begins with a sudden chill, fever, cough, and pleuritic pain. Sputum is a red or brown " rusty " color. Bacteremia occurs in 15-25% of cases. Spontaneous recovery may begin in 5-10 days and is accompanied by development of anticapsular antibodies. Pneumococci are a prominent cause of otitis media, sinusitis, purulent bronchitis, bacterial meningitis, and sepsis, especially in immunocompromised patient.

مركز الشامل للخدمات الطلابية

Laboratory Diagnosis In sputum , pneumococci can be seen as predominant organisms in Gram - stained smears as Gram positive lancet shaped diplococci or in the quellung reaction with multitype antiserum. On blood agar, pneumococci form small **alpha - hemolytic** colonies. The colonies are **bile - soluble** , ie, are lysed by bile , and growth is **inhibited by optochin**. Blood cultures are positive in 15 - 25% of pneumococcal infections. Culture of cerebrospinal fluids is usually positive in meningitis.

BECAUSE OF THE INCREASING NUMBERS OF STRAINS RESISTANT TO PENICILLIN ANTIBIOTIC SENSITIVITY TESTS MUST BE DONE ON ORGANISMS ISOLATED FROM SERIOUS INFECTIONS.

Treatment Most pneumococci are susceptible to penicillins and erythromycin. In severe pneumococcal infections, penicillin G is the drug of choice , whereas in mild pneumococcal infections, oral penicillin V can be used. In penicillin - allergic patients, erythromycin or one of its long - acting derivatives, eg, azithromycin, can be used. In the United States, about 25% of isolates exhibit low level resistance to penicillin, primarily as a result of changes in penicillin - binding proteins. An increasing percentage of isolates, about 7% currently, show high- level resistance, which is attributed to multiple changes in penicillin - binding proteins. **They do not produce β - lactamase**. Vancomycin is the drug of choice for the penicillin - resistant pneumococci. However, strains of pneumococci tolerant to vancomycin have emerged. (tolerance to antibiotics is described on p 70).

Prevention Despite the efficacy of antimicrobial drug treatment , the mortality rate is high in elderly (ie, persons older than 65 years), immunocompromised (especially splenectomized) or debilitated persons. Such persons should be immunized with the polyvalent (23 - type) polysaccharide vaccine. The vaccine is safe and fairly effective and

Handwritten notes:

- Analysis
- St. bovis
- E. faecalis
- penicillin G
- Not 65%
- Bile growth differentiation.

مركز الشامل للخدمات الطلابية

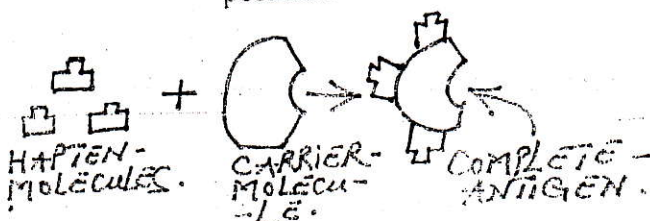
provides long – lasting (at least 5 years) protection. A booster dose is recommended for (1) people over the age of 65 who received the vaccine more that 5 years ago and who were less than 65 when they received the vaccine and (2) people between the ages of 2 and 64 who are asplenic, HIV – infected, receiving cancer chemotherapy, or receiving immunosuppressive drugs to prevent transplant rejection. Oral penicillin is given to young children with hypogammaglobulinemia or splenectomy because such children are prone to pneumococcal infections and respond poorly to the vaccine. (**HAPTENS**) .

In 1998, a vaccine containing pneumococcal polysaccharide **coupled to a carrier protein (diphtheria toxoid)** as the immunogen was shown to be effective in young children in preventing meningitis and otitis media. The vaccine contained the polysaccharide of the seven most common pneumococcal serotypes. This vaccine was approved by the FDA in February 2000 , + treatment of carriers + avoid predisposing factors.

1976

REVIEW QUESTIONS

1. What are the differences in appearance on gram – stained smears between staphylococci, streptococci, and pneumococci?
2. What is the typical pathologic lesion caused by staphylococci?
3. What laboratory test distinguishes *Staphylococcus aureus* from *Staphylococcus epidermidis*?
4. Which staphylococcal species is usually associated with (a) endocarditis in drug addicts, (b) endocarditis in patients with prosthetic heart valves, (c) osteomyelitis, (d) lower urinary tract infections, and (e) carbuncle ?
5. What is the pathogenesis of staphylococcal food poisoning ?
6. What are the virulence factors produced by *S aureus*, and what is their postulated mode of action.?



7. Many *S. aureus* infections are unsuccessfully treated with benzylpenicillin (penicillin G). Why?
8. Distinguish between the grouping and typing of streptococci.
9. Which streptococcal species is usually associated with (a) pharyngitis, (b) neonatal sepsis, (c) infective (subacute) endocarditis, (d) pyoderma, (e) urinary tract infection, (f) glomerulonephritis, and (g) rheumatic fever?
10. What is the role of hemolysis in the classification of streptococci?
11. What are the natural habitat and special growth characteristics of enterococci?
12. What is the role of each of the following virulence factors in the production of disease by *Streptococcus pyogenes*? (a) hyaluronidase; (b) M protein, ; (c) erythrogenic toxin.
13. Describe the pathogenesis of (a) rheumatic fever and (b) acute glomerulonephritis.
14. How is *Streptococcus pyogenes* (group A) distinguished from *Streptococcus agalactiae* (group B) in the clinical laboratory?
15. How are pneumococci (*Streptococcus pneumoniae*) and viridans streptococci distinguished in the clinical laboratory ?
16. Pneumococci have many serologic types. What is the nature of the antigen, and what role does it play in pathogenesis ?
17. What is the pathogenesis of pneumococcal pneumonia?
18. How can pneumococcal pneumonia and bacteremia be prevented?

Association of class II human histocompatibility leukocyte antigens with rheumatic fever.

(*Streptococcus - pyogenes*).

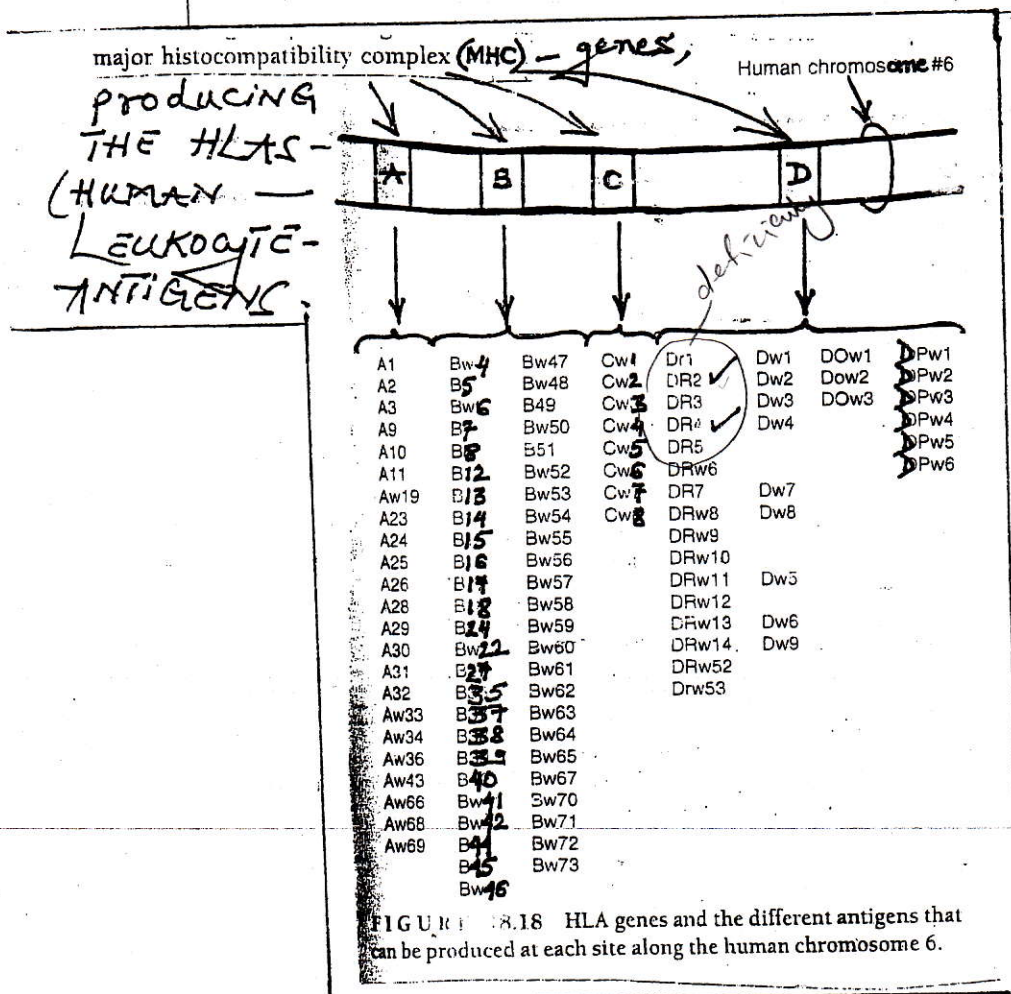


Fig. 30.2

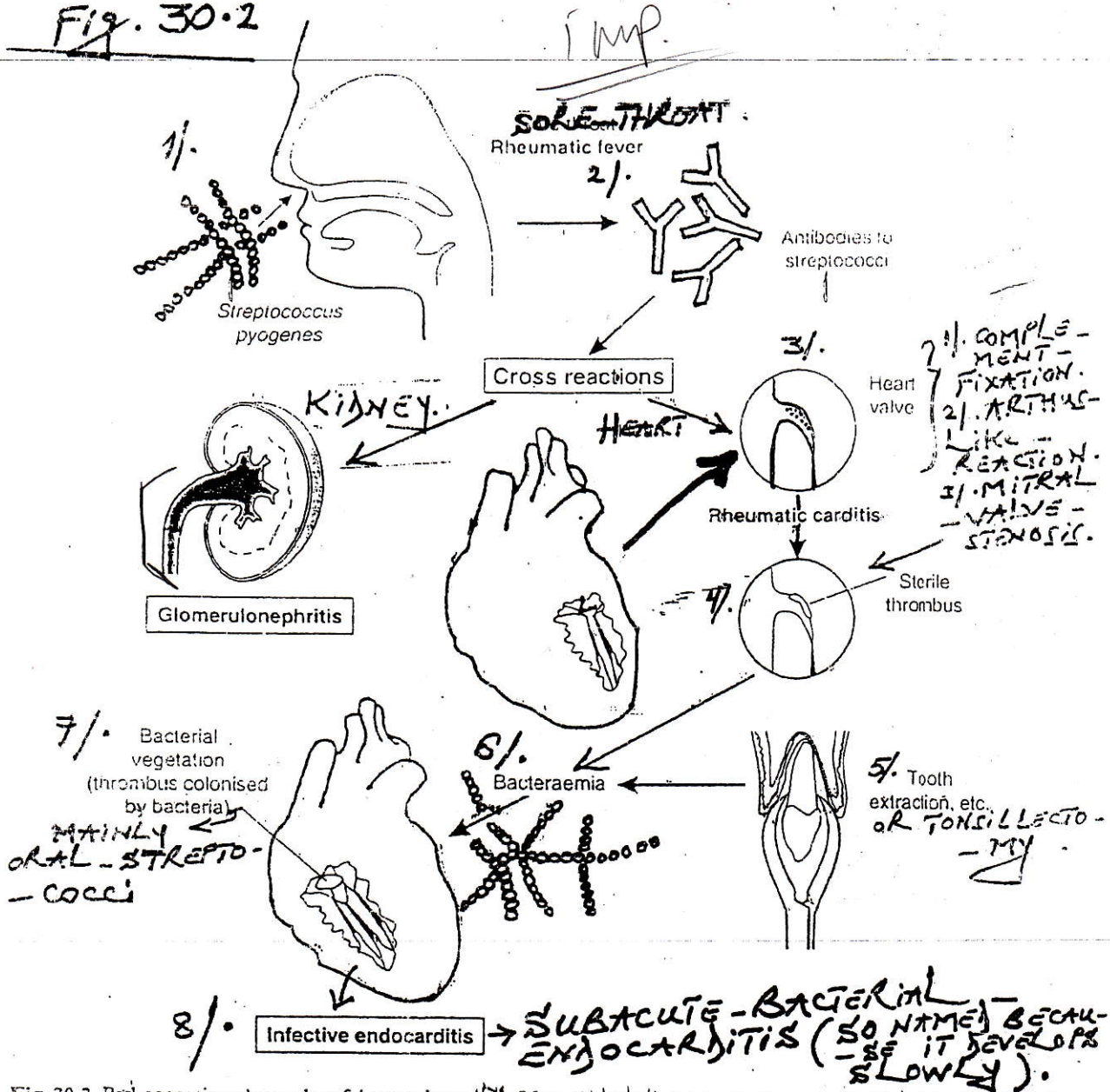


Fig. 30.2 Pathogenesis and sequelae of rheumatic carditis. (Note. Events leading to infective endocarditis are also illustrated.)

CAMP - TEST

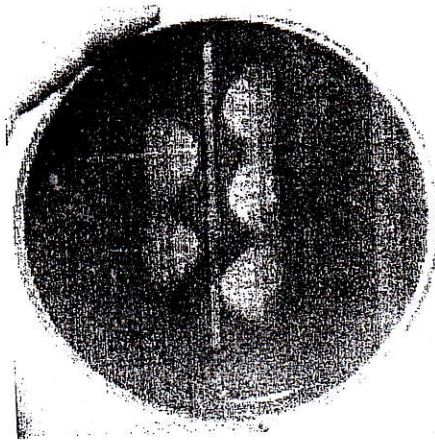
- CAMP is an acronym for ~~Christie, Atkins, Munch, Peterson~~, the discoverers of this phenomenon.
- This procedure is used to confirm that a bacterial strain is a Group B streptococci by production of a characteristic zone of hemolysis when grown in proximity to *S. aureus*.

Procedure:

1. Using an inoculating needle or the edge of a loop, streak *S. aureus* in a straight line down the center of a BAP.
2. Streak strains of suspected streptococci at right angles to the *S. aureus* 2-3 cm apart.
3. Be careful to streak the streptococcal strains close to, but not touching, the *S. aureus* streak. Label and incubate at 37° C.

Results: Observe for signs of enhanced hemolysis in the shape of an "arrowhead" where the *S. aureus* and streptococcal growth are in the nearest proximity.

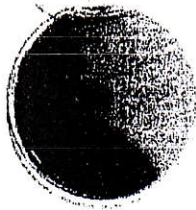
The weak beta-hemolysis of Group B Strep (*Streptococcus agalactiae*) synergistically combines with the beta hemolysis of a strain of *Staph aureus* to produce the arrow head shape of strong beta hemolysis that characterizes a positive CAMP test (named for the initials of the 4 discoverers).



Microbiology Primer: Hemolysis

There are two types of hemolysis on blood agar plates: alpha, beta, and gamma (gamma-hemolysis is actually no-hemolysis).

Alpha hemolysis



Streptococcus pneumoniae

Beta hemolysis

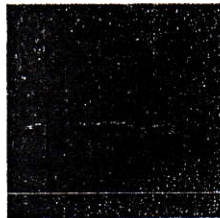


Streptococcus pyogenes
(Group A beta-hemolytic strep)

Gamma hemolysis



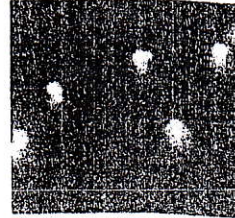
Enterococcus faecalis
(formerly Group D Strep)



There is a darkening of the agar.



There is complete lysis of red cells. Light will shine through an area of beta-hemolysis. In the thick part of the streak on this plate, one can see the label through the clearing.



There is no change of the agar. But note: Some strains of Strep exhibit alpha hemolysis limited to underneath the colony. These may be initially misidentified as gamma Strep.

For comparison, here are the above three strains streaked out on the same plate.



Certain species of bacteria are weakly beta-hemolytic but synergize with a strain of Staph to produce intense beta-hemolysis. This is called the CAMP test (after the initials of its inventors). One such species is Group B Strep (*Streptococcus agalactiae*).



2 tests
to differentiate
Pyogenes
Agalactiae
Bacitracin
and
CAMP test

Optochin
Disc
differentiate
Pneumonia
and
oral

POSITIVE - RESULT AND NEGATIVE - RESULT OF CAMP - TEST: -

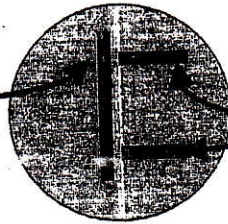
imp.

Fig 33.

SET UP

Solidifying Agent
clotting

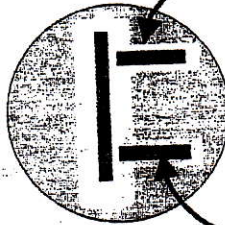
Staph. aureus
streak line



unknown isolates
(identify on the bottom of the
plate and incubate at 37C for
18-24 hours)

READ REACTIONS

Staph. aureus will produce 2
zones of hemolysis .



Positive CAMP test at 18-24
hours. Note the exaggerated
zone of beta-hemolysis
(white area) at the junction of
the 2 streak lines

Negative CAMP test at 18-24
hours. Note the absence of
any exaggerated zone of
beta-hemolysis at the
junction of the 2 streak lines.

Table 15-4B

Esculin' agar

Ready-to-use medium
4 136 4 Sachet of 5 tubes

Formula in g/l of distilled water	
bio-Tryptase	17
bio-Thione	3
Yeast extract	5
Ox bile	10
Sodium chloride	5
Sodium citrate	1
Esculin	1
Ammonium iron citrate	0.5
Sodium azide	0.25
Agar	13.5
pH 7.1	

Esculin agar is used for the detection of hydrolyzed esculin. The liberated compounds react with iron salts to give an easily detectable black color and so helps in the differentiation between *Listeria monocytogenes* and *Erysipelothrix rhusiopathiae*.

USE

Inoculate the tubes by a central stab using a platinum wire. Incubate at 37° C for 24-48 hours or 3-4 days for delayed reactions.

READING

Positive reaction: blackening of the tube

Negative reaction: no blackening

If the reaction is doubtful, compare with a non-inoculated tube also incubated under the same conditions.

[+] reaction: *Listeria monocytogenes*, *Streptococcus D*, *Serratia marcescens*, *Yersinia pseudotuberculosis*, *Yersinia pestis*, *Enterobacter aerogenes*, *Klebsiella pneumoniae* and *K. oxytoca*.

[±] reaction: *Erysipelothrix*, *Salmonella*, *Shigella*, *Staphylococci* etc.

1. Esculin is a 7-
dihydrocoumarin-6-
glucoside from
HORSE-CHESTNUT BARK.

PHYSIOLOGICAL - CHARACTERISTICS OF

Enterococcus faecalis : -

LABORATORY - TESTS : -	RESULTS:-
1/. GROWTH IN MacCONKEY-AGAR. (10% BILE-SALTS).	YES.
2/. GROWTH IN A MEDIUM = PH 9.6.	YES.
3/. GROWTH IN A MEDIUM OF 6.5% SODIUM - CHLORIDE.	YES.
4/. GROWTH IN 40% - BILE - SALTS - MEDIUM.	YES.
5/. SURVIVAL - AT 60°C FOR 30 - MINUTES.	YES.
6/. SENSITIVITY TO PENICILLIN.	RESISTANT.

Antistreptolysin O Titer (ASO Titer)

Normal Findings

Adult/elderly: 160 Todd units/ml

Child

6 months to 2 years: 50 Todd units/ml

2-4 years: 160 Todd units/ml

5-12 years: 170-330 Todd units/ml

Newborn: similar to mother's value

Indications

This test is used primarily to determine whether a previous *Streptococcus* infection has caused a poststreptococcal disease, such as glomerulonephritis, rheumatic fever, bacterial endocarditis, and scarlet fever. Levels are highest in glomerulonephritis and rheumatic fever.

Test Explanation

The ASO titer is a serologic procedure demonstrating the reaction of the body to infection caused by group A beta-hemolytic streptococci. The *Streptococcus* organism produces an enzyme called streptolysin O, which has the ability to destroy (lyse) red blood corpuscles. Because streptolysin O is antigenic, the body reacts by producing ASO, a neutralizing antibody. ASO appears in the serum 1 week to 1 month after the onset of a streptococcal infection; a high titer is not specific for a certain type of poststreptococcal disease (i.e., rheumatic fever vs. glomerulonephritis) but merely indicates that a streptococcal infection is or has been present. When ASO elevation is seen in a patient with glomerulonephritis or endocarditis, one can safely assume that the disease was caused by streptococcal infection. ASO is of no value for diagnosing acute streptococcal infection. Cultures for streptococci are required for that. However, cultures are useless during the latent period of the poststreptococcal disease (about 2 to 3 weeks after initial infection). ASO is very helpful at this point. Serial ASO testing may be performed to detect the difference between the acute and convalescent blood sample. Serial rising titers of ASO over several weeks, followed by a slow fall in titers, is much more significant in the diagnosis of a previous streptococcal infection than is a single titer. The highest incidence of positive results is during the third week after the onset of acute symptoms of the streptococcal disease. By 6 months, only about 30% of patients have abnormal titers.

Another immunologic test, antideoxyribonuclease-B (anti-DNase-B) (p. 61), also detects antigens produced by group A streptococci. The anti-DNase-B level is elevated in most patients with acute rheumatic fever and poststreptococcal glomerulonephritis. When ASO and anti-DNase-B are performed concurrently, 95% of previous streptococcal infections are detected. If both are repeatedly negative, there is no reason to suspect the symptoms are caused by a poststreptococcal disease. The Streptozyme test is often used as a screening test to detect any one of multiple streptococcal-induced antibodies.

Interfering Factors

- Increased beta-lipoprotein levels can neutralize streptolysin O and can cause a false-positive ASO titer.
- ✓ Drugs that may cause *decreased* ASO levels include antibiotics and adrenocorticosteroids. Antibiotics reduce the number of streptococci and thereby suppress ASO production. Steroids are immunosuppressive and thereby suppress ASO production.

Procedure and Patient Care

Before

- Explain the procedure to the patient.
- Tell the patient that no fasting is required.

During

- Collect approximately 5 to 10 ml of blood in a red-top tube.
- Avoid hemolysis of the blood specimen.
- Note on the laboratory slip any medications that may affect the test results.

After

- Apply pressure or a pressure dressing to the venipuncture site.
- Observe the venipuncture site for bleeding.
- Note that repeat ASO testing may be done to determine the highest level of increase.

Test Results and Clinical Significance :

Increased levels :

Acute streptococcal infection *ASO titers will not have developed during the early days of the infection. It is only after the second week of an untreated infection that the ASO will rise.*

Acute rheumatic fever

Bacterial endocarditis

ASO titers are highest in these diseases.

Acute glomerulonephritis *As many as 50% to 75% of these patients will not have high ASO titers.*

Scarlet fever

Streptococcal pyoderma

ASO is often not elevated in these diseases.

Related Tests :

- Antideoxyribonuclease-B titer (p. 61): Like the ASO test, this immunologic test also detects antigens produced by group A streptococci and is positive in most patients with acute rheumatic fever or poststreptococcal glomerulonephritis. •

End